

APPLN. FILING DATE: JANUARY 26, 2004
TITLE: GOMPOSITION FOR AND TREATMENT OF
DEMYELINATING DISEASES AND PARALYSIS BY
ADMINISTRATION OF REMYELINATING AGENTS
INVENTOR(S): STEVE J. KARLIK ET AL.
APPLN. NO.: 10/763,539
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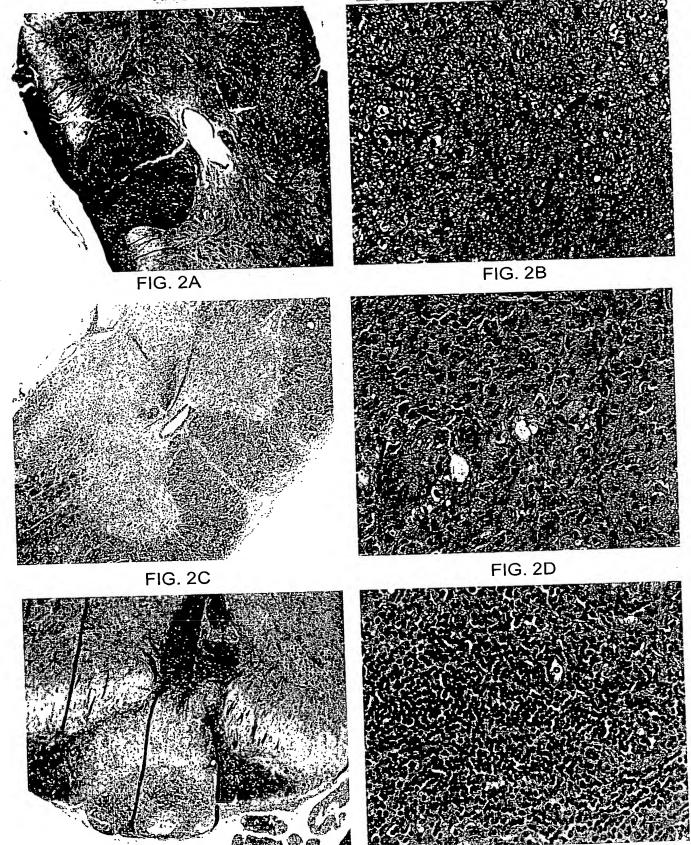


FIG. 2E

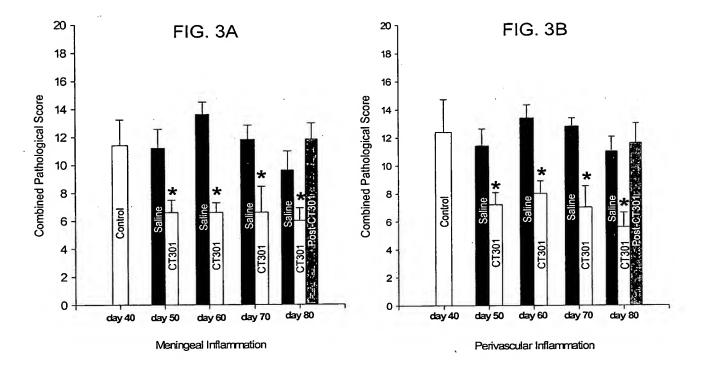
FIG. 2F

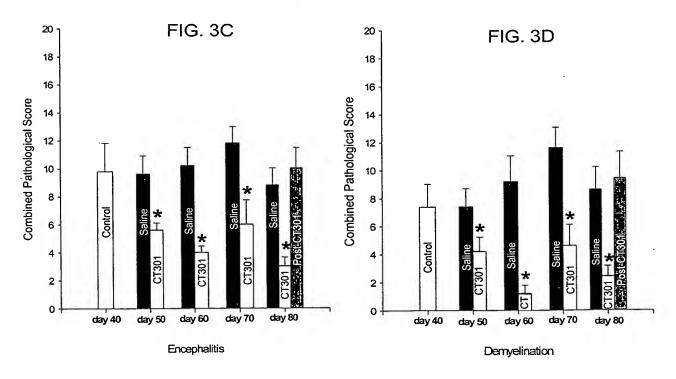
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SHEET 3 OF 25 **SHEET 3 OF 25** FIG. 2H FIG. 2G FIG. 2J FIG. 21

FIG. 2K

FIG. 2L

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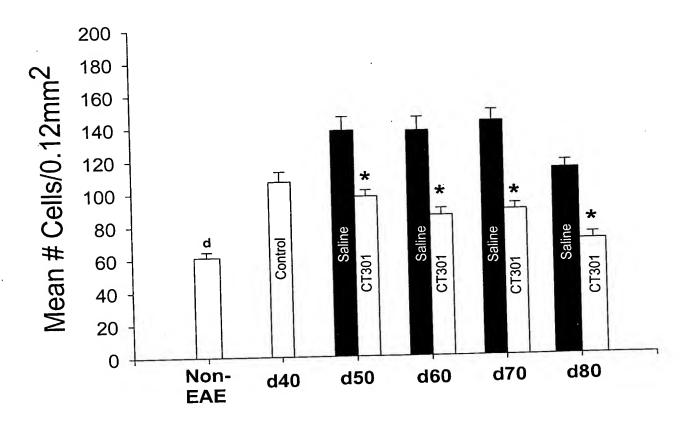
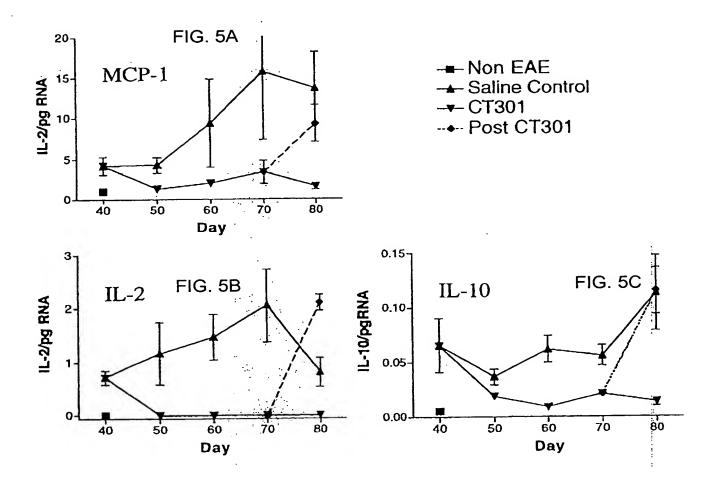


FIG. 4

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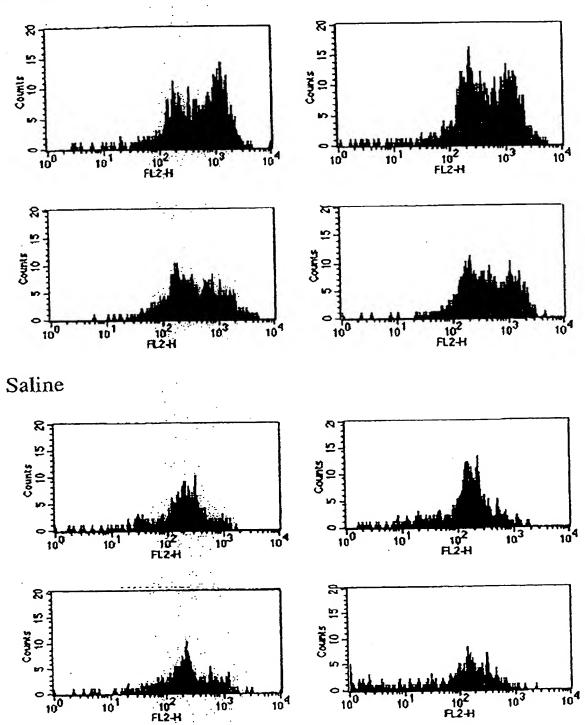


FIG. 6

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## Percentage $\alpha 4$ Integrin-High **Blood Lymphocytes**

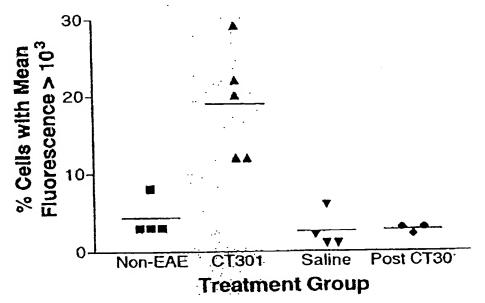


FIG. 7A

## Expression of $\alpha 4$ Integrin on **Blood Monocytes**

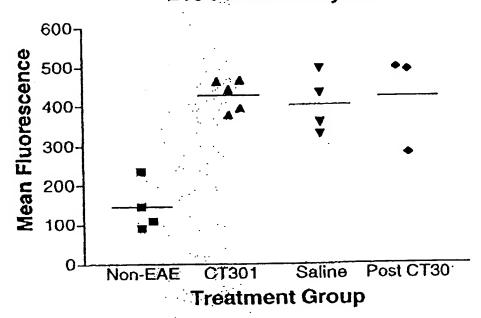


FIG. 7B

- Non-EAE
- CT301
- Saline
- Post CT301

Non-EAE

Post CT301

CT301

Saline

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FIG. 8

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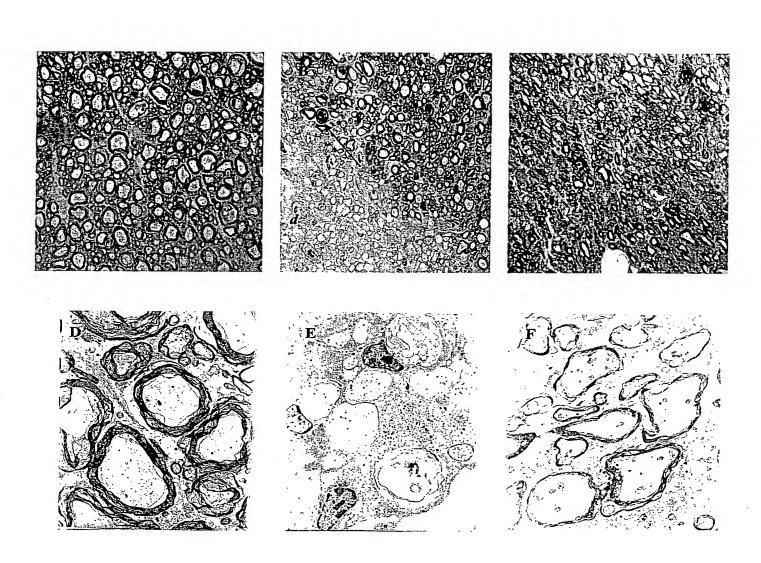
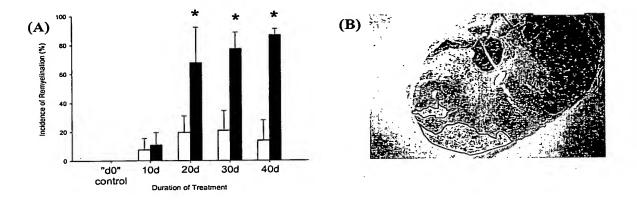
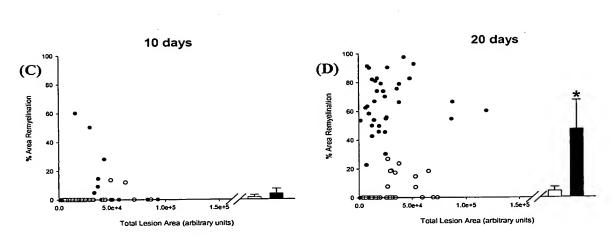


FIG. 9

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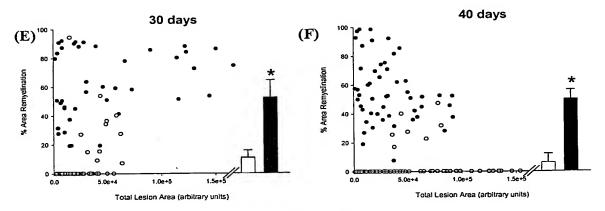


FIG. 10

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atgagggcccctgctcagatttttggattcttggtcaggagacgttgt

l ----tactcccggggacgagtctaaaaacctaagaaccagtcctctgcaaca

agaaatgagaccgtctattcagttcctggggctcttgttgttctggcttcatgg
49 ----tctttactctggcagataagtcaaggaccccgagaacaacaagaccgaagtacc

[M R P S I Q F L G L L F W L H G LEADER

A Q C][D I Q M T Q S P S S L S A S L gggaggcaaagtcaccatcacttgcaagacaagccaagacattaacaagtatat ccctccgtttcagtggtagtgaacgttctgttcggttctgttaattgttcatata

G G K V T I T C] [K T S Q D I N K Y M CDR1

ggcttggtaccaacacaagcctggaaaacgtcctaggctgctcatacattacac
211 -----ccgaaccatggttgtgttcggaccttttgcaggatccgacgagtatgtaatgtg

A] [W Y Q H K P G K R P R L L I H] [Y T FR2

atctgcattacagccaggcatcccatcaaggttcagtggaagtgggtctgggag
265 ----tagacgtaatgtcggtccgtagggtagttccaagtcaccttcacccagaccctc

S A L Q P][G I P S R F S G S G S G R

FIG. 11 A

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agattattccttcaacatcagcaacctggagcctgaagatattgcaacttatta 319 -tctaataaggaagttgtagtcgttggacctcggacttctataacgttgaataat DIA E ₽ S FR3 ttgtctacagtatgataatctgtggacgttcggtggaggcaccaagctggaaat 373 aacagatgtcatactattagacacctgcaagccacctccgtggttcgaccttta W T][F G G G T K Y D N C][L Q FR4 CDR3 caaacgggctgatgctgcaccaactgtatccatcttcccaccatccacccggga 427 ----gtttgcccgactacgacgtggttgacataggtagaagggtggtaggtggccct K]

AGG-5' tcc 481 --agg

		•																
		1		gaa	arg	cag	ctg	ggt	cato	gtt	ctt	cct	gat	ggc	agt	ggt	tac	aggg
		1		ctt	tac	gtc	gac	cca	gtad	caa	gaa	gga	cta	cca.	cca	cca	atg	tccc
						•	•											
	•		(M	K	С	s	W	V	М	F L	F EADI	L ER	М	A	V	<b>v</b> .	T	G .
40	gt	caa	ttc	aga	ggtı	ca	gct	gca	gca	gtc	cgg	ggca	agaq	gct <sup>.</sup>	tgt	gaa	gcc	aggg
. 49	cagttaagtctccaagtcgacgtcgtcagaccccgtctcgaacacttcggtccc																	
	<b>v</b>	N		(E	V	Q ·	L	Q	Q	s	G	A	E	L	v	K R1	P	G
103	gc	ctc	agt 	caad	gtto	gtc:	ctg:	caca	agct	:tc1		ctto	caac	ati	taa	aga	caco	ctat
	cg	gag	tca	gtt	caac	cago	gac	gtgt	cga	aaga	acco	gaaç	gttç	gta	att.	tct	gtg	gata
	A	s	v	K	L	s	С	T	A	s	Ģ	Ę	N .	ı.	K]	[D	T CI	Y OR1
	ata	aca	ctg	tgt	jaaq	gcaq	gag	gcct	gaa	caq	ggg	cctq	ggag	, t.g	gati	t gga	aago	gatt
157	atacactgtgtgaagcagaggcctgaacagggcctggagtggattggaaggatt																	
	į	H]		V	к	Q	R	P	E	Q.	G R2	L	E	W	I	G]		I
211	gat	cc	tgc	gaat	ggt	tat	act	caaa	itat	gad	ccé	gaag	jttc	caq	3330	caaç	ggc	cact
	cta	agg	acg	ctta	ıcca	aata	atga	attt	ata	ct	3990	t t	aag	gto	cc	gtt o	cg	gtga
	<b>D</b>	P	Ä	N	G	Y CDF	T R2	K	Y	D	P	K	F	Q	G]	(K	Α	T
265	ata	ac	agcı	gac	aca	atco	ctc	caac	aca	gc	tac	ctg	rcag	cto	ago	cago	ctç	gaca
265	tat	tg	tcg:		 Itgt	ago	gagg		 jtgt	cg	at o	gac	gto	gad	i	gtc	gac	tgt
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FIG. 12A

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totgaggacactgccgtctatttctgtgctagagagggatattatggtaactac agactcctgtgacggcagataaagacacgatctctccctataataccattgatg A R][E G F C Y G CDR3 ggggtctatgctatggactactggggtcaaggaacctcagtcaccgtctcctca 373 -ccccagatacgatacctgatgaccccagttccttggagtcagtggcagaggagt M D Y] [W G Q gccaaacgacaccccatctgtctatccactggcccgggatcc 427 cggttttgctgtgggggtagacagataggtgaccgggccctagg S]

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	FR1	CDR1	FR2	CDR2
	1 2	3	4	5
	12345678901234567890123	45678901234	567890123456789	0123456 ***
21.6	DIQMTQSPSSLSASLGGKVTITC	KTSQDINKYMA	WYQHKPGKRPRLLIH	YTSALQP
REI	DIQMTQSPSSLSASVGDRVTITC	QASQDIIKYLN	WYQQTPGKAPKLLIY	EASNLQA
La	DIQMTQSPSSLSASVGDRVTITC	KTSQDINKYMA	WYQQTPGKAPRLLIH	YTSALQP
Lb			R	
	v .		-	
	FR3	•	CDR3 FR4	

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		FR1 .		CDR1	FR2		CDR2	
	1	. 2	3		4	5		6
	123456789012	34567890123	34567890 *****	12345	6789012345		A345678! ****	9012345
21.6	EVQLQQSGAELV	KPGASVKLSC1	rasgfnik	DIYIH	CVKQRPEQGL	EWIG RID	PANGYTK	YDPKFQĞ
2*CL	QVQLVQSGAEVK	KPGASVKVSCI	KASGYTFT	SYAMH	WVRQAPGQRL	EWMG WIN	AGNGNTK	YSQKFQG
На	QVQLVQSGAEVK	KPGASVKVSC	KASG <u>FNIK</u>	DTYIH	WVRQAPGQRL	EWMB RID	PANGYTK	YDPKFQG
НЬ			FNIK	·	G-			
НС			FNIK					
-			-				•	
		FR3			CDR3	FR4		
	. 7	8	9	-	10	1	1	
	678901234567	89012ABC34	56789012	34 5678 *	390ABCDEF12	3456789	0123	
21.6	KATITADTSSNT	AYLQLSSLTSI	EDTAVYFC	AR EGY	YGNYGVYAMDY	WGQGTSV	TVSS	
2*CL	RVTITRDTSAST	AYMELSSLRSI	EDTAVYYC	AR GGY	GSGSNY	WGQGTLV	TVSS	
Ha .	RVTIT <u>A</u> DTSAST	AYMELSSLRSI	EDTAVYYC	AR EGY	/GNYGVYAMDY	WGQGTLV	TVSS	
НБ	A							
Нс	A			E	r			

ADMINISTRATION OF REMYELINATING AGENTS INVENTOR(S): STEVE J. KARLIK ET AL.
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FIG. 15A

FR3

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K V E I K]

ttcCACctttagtttgcactcacctagg

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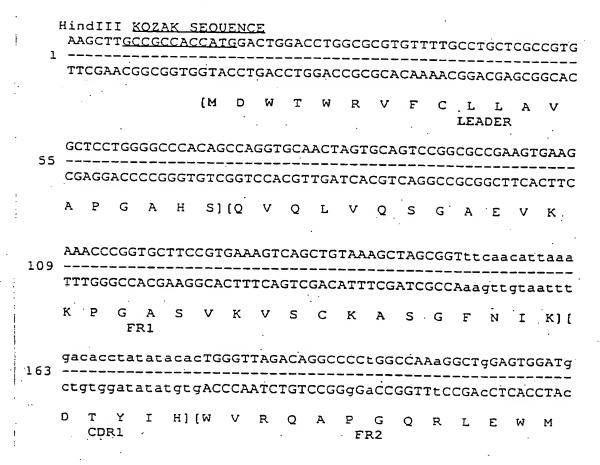


FIG. 16A

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217	GGaaggattgatcctgcgaatggttatactaaatatgacccgaagttccagggc																	
	CCttcctaactaggacgcttaccaatatgatttatactgggcttcaaggtcccg																	
:	G]	[R	I	D <sub>.</sub>	5	A	N	G	Y	T	K CDR	Y 2	.D	p	K	F	Q	G].[
	cgggtcACCatcACCgcaGACACCTCTgccagcACCGCCTACATGGAACTGTCC																	
271	gcccagTGGtagTGGcgtCTGTGGAGAcggtcgTGGCGGATGTACCTTGACAGG																	
	R	V	т	I.	Т	A	Ď	Τ	s	A	s	T	A	<b>Y</b>	М	E	L,	S FR3
325	AGCCTGCGCTCCGAGGACACTGCAGTCTACTACTGCGCCagagagggatattat													ttat				
	TC	GGA	CGC	GAGO	GCT	CT	GTG.	ACG'	rca(	GAT	GAT	GAC	GCG	Gtc	tct	ccc.	tat	aata
	s	Ĺ	R	s,	E	D	T	A <sub>.</sub>	V	Y	Y	С	A	R]	(E	G	Y	Y
379	<b>aa</b> .	taa	cta	cggg	gt	cta	tgc 	tat	gGA	CTA	CTG	GGG	tCA	aGG	aAC(	CCT	TGT	CACC
	ccattgatgccccagatacgatacCTGATgACCCCaGTtCCtTGGGAACAGTGG																	
1	G	N	Y CDR:		v	Y	A	M <sub>j</sub>	Ď	YJ	W)	G	Q	G	T	L F	V R4	T
			E DO															
;433 !	CA	Gag	gAG:	rcc:	ACT	CAC	CTA	GG						-				
:	v	s	51															

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(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 109 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- N Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Leu Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Asp Ile Ser Asn Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Gly Ser Pro Lys Leu Leu Ile Tyr Tyr Ala Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Ser Asn Leu Glu Gln Glu Asp Ile Ala Thr Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Pro Arg Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys C

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(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 114 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

N - Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ser Leu Val Xaa Xaa Ser Ile Ser Asn Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Asn Ser Leu Pro Glu Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys - C

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APPLN. No.: 10/763,539
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(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 125 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein
- N Glu Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Lys Pro Gly Ala Ser Val Lys Leu Ser Cys Thr Ala Ser Gly Phe Asn Ile Lys Asp Thr Tyr Met His Trp Val Lys Gln Arg Pro Glu Gln Gly Leu Glu Trp Ile Gly Arg Ile Asp Pro Ala Asn Gly Asn Thr Lys Tyr Asp Pro Lys Phe Gln Gly Lys Ala Thr Ile Thr Ala Asp Thr Ser Ser Asn Thr Ala Tyr Leu Gln Leu Ser Ser Leu Thr Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Gly Tyr Tyr Tyr Asp Ser Xaa Val Gly Tyr Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Xaa Val Thr Val Ser Ser C

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(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 129 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein

```
N - Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr Ala Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met Gly Trp Ile Asn Pro Tyr Gly Asn Gly Asp Thr Asn Tyr Ala Gln Lys Phe Gln Gly Arg Val Thr Ile Thr Ala Asp Thr Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Ala Pro Gly Tyr Gly Ser Gly Gly Gly Cys Tyr Arg Gly Asp Tyr Xaa Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser - C
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